

**CLAIMS**

I claim:

1. A method of diagnosing and treating a patient with or  
5 suspected of having at least one solid tumor that produces folate receptor  $\alpha$   
comprising administering a biologically effective amount of at least one  
folate receptor  $\alpha$  inducer, the at least one folate receptor  $\alpha$  inducer  
comprising at least one steroid receptor agent, optionally together with one  
or more histone deacetylase inhibitors, wherein the at least one folate  
10 receptor  $\alpha$  inducer increases levels of folate receptor  $\alpha$  on plasma  
membranes of tumor cells as well as folate receptor  $\alpha$  in at least one type of  
body fluid.
2. The method of claim 1, wherein the body fluid includes at least  
15 one of serum, ascites and cerebrospinal fluid
3. The method of claim 1, wherein a diagnostic assay is  
performed using samples of said body fluid.
- 20 4. The method of claim 1, wherein diagnostic tumor imaging is  
performed using at least one imaging agent directed at folate receptor  $\alpha$ .
5. The method of claim 1, wherein the patient is treated by  
administering a therapeutic agent that targets folate receptor  $\alpha$  expressed  
25 by tumor cells.
6. The method of claim 1, wherein the steroid receptor  
comprises at least one of estrogen receptor (ER), progesterone receptor  
(PR), androgen receptor (AR) or glucocorticoid receptor (GR).

7. The method of claim 1, wherein the folate receptor  $\alpha$  inducer comprises at least one or more agonist or antagonist agent of at least one steroid receptor.

5 8. The method of claim 7, wherein the steroid receptor agent comprises at least one of tamoxifen, progestin, androgens and dexamethasone and optionally, any other agent that acts on estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR) or glucocorticoid receptor (GR).

10 9. The method of claim 8, wherein the diagnosis and/or treatment of a patient comprises administering at least one histone deacetylase inhibitor to the patient together with one or more steroid receptor agonists or antagonists wherein the histone deacetylase inhibitor includes at least one of  
15 trichostatin A (TSA), suberoylanilide hydroxamic acid (SAHA), depsipeptide, valproic acid, butyrates, or other HDAC inhibitor.

20 10. The method of claims 1 through 9, wherein a composition for assaying folate receptors in serum and ascites comprises at least one of fluorescent conjugates of folate or antibodies specific for the folate receptor is used.

25 11. The method of claims 1 through 9, wherein a composition for therapeutic targeting of the folate receptor comprising at least one of folate-coated liposomal drugs, folate conjugated nanoparticle drug delivery systems, antifolate drugs, folate conjugated radiopharmaceuticals or cytotoxics, or folate receptor-targeted immunotherapeutics is used.

30 12. The method of claim 6, wherein the steroid receptor comprises the glucocorticoid receptor (GR).

13. The method of claim 12, wherein the steroid receptor agent comprises dexamethasone or other GR agonist.

14. A method for diagnosing and/or therapeutically treating a patient comprising activating the FR- $\alpha$  gene in the patient using at least one of an agonist or antagonist of estrogen receptor (ER), progesterone receptor (PR), glucocorticoid receptor (GR) or androgen receptor (AR).

15. The method of claim 14, wherein the agonist or antagonist comprises at least one of tamoxifen, progestin, androgens and dexamethasone and optionally, any other steroid receptor agent that acts on estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR) or glucocorticoid receptor (GR).

16. The method of claim 15, wherein the steroid receptor comprises glucocorticoid receptor (GR) and the steroid receptor agent comprises dexamethasone or other GR agonist.

17. The method of claim 16, further comprising administering at least one histone deacetylase inhibitor.

18. The method of claim 15, wherein the steroid receptor comprises estrogen receptor (ER) and the steroid receptor agent comprises tamoxifen.

19. The method of claim 18, further comprising administering at least one histone deacetylase inhibitor.

20. The method of claim 15, wherein the steroid receptor comprises androgen receptor (AR) and the steroid receptor agent comprises at least one of testosterone, dihydroxytestosterone or other AR agonist.

21. The method of claim 20, further comprising administering at least one histone deacetylase inhibitor.

5        22. The method of claim 15, wherein the steroid receptor comprises progesterone receptor (PR) and the steroid receptor agent comprises progestin or other PR agonist.

23. The method of claim 20, further comprising administering at  
10    least one histone deacetylase inhibitor.

24. A method for substantially increasing folate receptor (FR) type  $\alpha$  expression in a tumor comprising using at least one steroid receptor agent, individually or in combination, to substantially increase folate receptor  
15    (FR) type  $\alpha$  expression in the tumor in a manner selective to FR- $\alpha$ -positive tissues.

25. The method of claim 24, wherein the steroid receptor agent comprises at least one agonist or antagonist including tamoxifen, progestin,  
20    androgens and dexamethasone and optionally, any other steroid receptor agent that acts on estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR) or glucocorticoid receptor (GR).

26. The method of claim 25, wherein the steroid receptor  
25    comprises glucocorticoid receptor (GR) and the steroid receptor agent comprises dexamethasone.

27. The method of claim 26, further comprising administering at least one histone deacetylase inhibitor.

28. The method of claim 25, wherein the steroid receptor comprises estrogen receptor (ER) and the steroid receptor agent comprises tamoxifen.

5        29. The method of claim 28, further comprising administering at least one histone deacetylase inhibitor.

30. The method of claim 25, wherein the steroid receptor comprises androgen receptor (AR) and the steroid receptor agent comprises  
10 at least one of testosterone or dihydroxytestosterone or other AR agonist.

31. The method of claim 30, further comprising administering at least one histone deacetylase inhibitor.

15        32. The method of claim 25, wherein the steroid receptor comprises progesterone receptor (PR) and the steroid receptor agent comprises progestin or other PR agonist.

33. The method of claim 32, further comprising administering at  
20 least one histone deacetylase inhibitor.

34. A method of manipulation of tumor tissues comprising using at least one steroid receptor agent to enhance sensitivity of whole body imaging and therapeutic efficacy of FR-targeted agents in the treatment of  
25 cancer and to increase the level of FR- $\alpha$  in circulation.

35. The method of claim 34, wherein the steroid receptor agent comprises at least one agonist or antagonist including tamoxifen, progestin, androgens and dexamethasone and optionally, any other steroid receptor  
30 agent that acts on estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR) or glucocorticoid receptor (GR).

36. The method of claim 35, wherein the steroid receptor comprises glucocorticoid receptor (GR) and the steroid receptor agent comprises dexamethasone or other GR agonist.

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37. The method of claim 36, further comprising administering at least one histone deacetylase inhibitor.

38. The method of claim 35, wherein the steroid receptor  
10 comprises estrogen receptor (ER) and the steroid receptor agent comprises tamoxifen or other ER agonist or antagonist.

39. The method of claim 38, further comprising administering at least one histone deacetylase inhibitor.

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40. The method of claim 35, wherein the steroid receptor comprises androgen receptor (AR) and the steroid receptor agent comprises at least one of testosterone or dihydroxytestosterone or other AR agonist.

41. The method of claim 40, further comprising administering at least one histone deacetylase inhibitor.

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42. The method of claim 35, wherein the steroid receptor comprises progesterone receptor (PR) and the steroid receptor agent  
25 comprises progestin or other PR agonist.

43. The method of claim 42, further comprising administering at least one histone deacetylase inhibitor.

44. A method of enhancing sensitivity of whole body imaging and  
30 therapeutic efficacy of FR-targeted agents in the treatment of cancer comprising manipulating tumor tissues by using steroid receptor agents that bind to folate receptor  $\alpha$ .

45. The method of claim 44, wherein the steroid receptor agent comprises at least one agonist or antagonist including tamoxifen, progestin, androgens and dexamethasone and optionally, any other steroid receptor agent that acts on estrogen receptor (ER), progesterone receptor (PR),  
5 androgen receptor (AR) or glucocorticoid receptor (GR).

46. The method of claim 45, wherein the steroid receptor comprises glucocorticoid receptor (GR) and the steroid receptor agent  
10 comprises dexamethasone or other GR agonist.

47. The method of claim 46, further comprising administering at least one histone deacetylase inhibitor.

15 48. The method of claim 45, wherein the steroid receptor comprises estrogen receptor (ER) and the steroid receptor agent comprises tamoxifen or other ER agonist or antagonist.

49. The method of claim 48, further comprising administering at  
20 least one histone deacetylase inhibitor.

50. The method of claim 45, wherein the steroid receptor comprises androgen receptor (AR) and the steroid receptor agent comprises at least one of testosterone or dihydroxytestosterone or other AR agonist.  
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51. The method of claim 50, further comprising administering at least one histone deacetylase inhibitor.

52. The method of claim 45, wherein the steroid receptor  
30 comprises progesterone receptor (PR) and the steroid receptor agent comprises progestin or other PR agonist.

53. The method of claim 52, further comprising administering at least one histone deacetylase inhibitor.

54. A method for increasing levels of FR- $\alpha$  in a patient's circulation  
5 comprising manipulating tumor tissues by using steroid receptor agents that bind to folate receptor  $\alpha$ .

55. The method of claim 54, wherein the steroid receptor agent  
10 comprises at least one agonist or antagonist including tamoxifen, progestin, androgens and dexamethasone and optionally, any other steroid receptor agent that acts on estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR) or glucocorticoid receptor (GR).

56. The method of claim 55, wherein the steroid receptor  
15 comprises glucocorticoid receptor (GR) and the steroid receptor agent comprises dexamethasone or other GR agonist.

57. The method of claim 56, further comprising administering at  
20 least one histone deacetylase inhibitor.

58. The method of claim 55, wherein the steroid receptor  
comprises estrogen receptor (ER) and the steroid receptor agent comprises tamoxifen or other ER agonist or antagonist.

59. The method of claim 58, further comprising administering at  
25 least one histone deacetylase inhibitor.

60. The method of claim 55, wherein the steroid receptor  
30 comprises androgen receptor (AR) and the steroid receptor agent comprises at least one of testosterone or dihydroxytestosterone or other AR agonist.



61. The method of claim 60, further comprising administering at least one histone deacetylase inhibitor.

62. The method of claim 55, wherein the steroid receptor  
5 comprises progesterone receptor (PR) and the steroid receptor agent comprises progestin or other PR agonist.

63. The method of claim 62, further comprising administering at least one histone deacetylase inhibitor.

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62. A serum marker for diagnostic screening and monitoring of cancers during and after treatment comprising the composition of claim 9.

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